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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/142,524	09/09/1998	TOSHIO SONE	SPO-103	2300

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EXAMINER	
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ART UNIT	PAPER NUMBER
1644	39

DATE MAILED: 05/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/142,524	Applicant(s) SONE ET AL.	
	Examiner DiBrino Marianne	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2003 and 03 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,5,13,32-34 and 48-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *49-51* is/are allowed.

6)☒ Claim(s) *1,4,5,13,32,33,48 and 52-70* is/are rejected.

7)☒ Claim(s) *34* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *filed* 3/3/03.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicant's amendments filed 2/20/03 (Paper No. 36) and 2/3/03 (Paper No. 34) are acknowledged and have been entered.

2. Claims 1, 4, 5, 13, 32-34, 48 and 49-70 are presently being examined.

Applicant's amendments filed 2/20/03 (Paper No. 36) and 2/3/03 (Paper No. 34) have necessitated the following new grounds of rejection.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1, 4, 5, 13, 32, 33, 56, 58 and 60-70 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 56 are indefinite in the recitation of "has no cysteine residues" because it is not clear what is meant. SEQ ID NO: 36 recited in base claims 1 and 52 has a cysteine residue.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1, 4, 5, 13, 32-33, 48 and 52-70 are rejected under 35 U.S.C. § 103(a) as being unpatentable over WO 93/08280 (IDS reference) in view of WO 94/01560 (20 January 1994, pages 1-106), JP0804739 (20 Feb 1996) and Rogers et al (Molecular Immunology, Vol. 31 (13) pp 955-966, 1994).

WO 93/08280 teaches recombitope peptides comprising T cell epitope peptides of Cry j1 and Cry j 2, the two major allergens of C. japonica (especially abstract and page 13), the use of a therapeutic composition comprising the said recombitope peptides for administration to allergic individuals for stimulating T cells, and which does not bind IgE specific for the protein allergen (especially page 16, page 17 and pages 33-34, claims 1-3, 7, 11, 12, 17, 19, 21, 23, 24, 42, 45, 67). WO 93/08280 teaches introduction of KK or RR between T cell epitope regions for in vivo cleavage (especially paragraph spanning pages 19 and 20).

WO 93/08280 does not teach a polypeptide/therapeutic composition thereof in which at least one T cell epitope peptide comprises one of SEQ ID NO: 28-31, 36 and 57 of the instant application from Cry j 1 linearly bound to at least one T cell epitope peptide comprising SEQ ID NO: 97, 100, 101, 120, 121, 131 or 152 of the instant application from Cry j2, including with a proteolytic cleavage site in between epitopes, nor wherein one of the peptides has substituted amino acid residues, nor a method of treatment of cedar pollinosis using the said polypeptide/composition thereof.

WO 94/01560 teaches peptides comprising SEQ ID NO: 28-31, 36 and 57 of the instant application from Cry j 1 which are or comprise T cell epitopes (especially Figure 13, page 31). The WO 94/01560 document teaches linear polypeptides comprising at least two different T cell epitope regions from Cry j 1 joined to each other which do not substantially react with allergic human IgE (especially Abstract, page 4, lines 17-24, page 13, lines 12-20). WO 94/01560 teaches peptides comprising at least two regions, each region comprising at least two T cell epitopes of a Japanese cedar pollen protein allergen or comprising epitopes from peptides which are immunologically related (especially page 26, lines 25-31). WO 94/01560 further teaches a peptide analog or modified peptide in which amino acid residues have been substituted to increase solubility, enhance therapeutic or preventive efficacy or to enhance ex vivo or in vivo stability, i.e., to increase resistance to proteolytic degradation in vivo or to increase shelf life ex vivo, to modify immunogenicity or reduce allergenicity or to modify reaction with T cell receptors or MHC binding of the T cell epitopes (especially pages 22 and 23). WO 94/01560 teaches Cry j1 and Cry j 2 are the two major allergens of C. japonica, Japanese Cedar Pollen allergen protein.

JP08047392 teaches T cell epitope peptides consisting of SEQ ID NO: 97, 100, 101, 120, 121, 131 and 152 from Cry j2 (especially page 15, peptide numbers 14, 17, 18, 37, 38, 48 and 69, respectively).

Rogers et al teach a peptide-based immmunotherapeutic agent comprising a linear multi-epitope polypeptide with different T cell epitopes joined to each other, and wherein the said polypeptide does not substantially react with allergic human IgE, wherein said different T cell epitope regions are derived from two or more different allergen molecules and wherein said polypeptide reacts with peripheral lymphocytes from at least not less than 70% of said population patients sensitive to said allergens (especially Abstract; page 956; Table 2; page 961, column 1, second full paragraph; page 963, column 1, lines 6-9; page 964, column 1, first two full paragraphs; page 964, column 2, lines 24-29 and lines 60-71; page 965, lines 1-2). Rogers et al teach that their approach to a peptide-based immunotherapeutic agent can be generally applicable to the combination of multiple T cell epitope-containing sequences from one or more antigens into a single polypeptide chain, that a single antigen can have multiple T cell epitopes recognized in the atopic human population, and that the polypeptide can also be constructed using T cell epitopes from unrelated antigens or allergens from diverse sources (page 964, lines 60-71 and continuing onto page 965, lines 1-2). Rogers et al teach the importance of the human T cell reactivity to individual T cell epitopes being maintained in the said polypeptide agent (especially Abstract and page 961, column 2). Rogers et al teach that making said T-cell epitope-containing peptides which have significantly reduced reactivity with allergic human IgE is a novel and useful therapeutic approach for desensitization to important allergens.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made a recombitope peptide/composition thereof such as the one taught by WO 93/08280 comprising T cell epitopes of cryj1 and cry j2 using at least one of the T cell epitopes of cry j1 taught by WO 94/01560 and at least one of the T cell epitopes of cry j 2 taught by JP08047392, and which maintains the T cell reactivity to individual T cell epitopes in vitro and in vivo as taught by Rogers et al, and to have used it in the method taught by WO 93/08280 for administration to allergic individuals for stimulating T cells, i.e., for treatment of individuals with cedar pollinosis. One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to make T-cell epitope-containing peptides which have significantly reduced reactivity with allergic human IgE for use in desensitization to important allergens, such as treatment of pollenosis caused by Japanese Cedar Pollen, as taught by Rogers et al in order to treat pollenosis.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have constructed a multi-epitope peptide using lysine or arginine dimers that can be introduced between T cell epitope regions to serve as a site that is processed in antigen-presenting cells given the teaching of WO 94/01560 and of WO 93/08280 or to substitute amino acid residues of the T cell epitope peptides as taught by WO 94/01560. One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to enhance processing of the epitopes for presentation by HLA as taught by WO 94/01560 and to enhance efficacy, solubility or stability or to modify immunogenicity or reduce allergenicity as taught by WO 94/01560, respectively

During examination, claims are given their broadest reasonable interpretation. With regard to instant claim 13, the peptide consists of minimum core sequences depending upon which HLA molecule the T cell epitope peptides binds and which T cells are specific for the combination. With regard to instant claims 32 and 33, the HLA restriction of the T cell epitope peptides appears to be an expected property of the said peptides. With regard to instant claims 52-70, these claims are included in this rejection because the peptides taught by WO 94/01560 are T cell epitope peptides "comprising at least one T-cell epitope peptide consisting of an amino acid sequence" selected from the recited sequences in base claim 52. Instant claims 1, 4, 5, 13, 32, 33, 48, 56, 58, 60, 61-70 are included in this rejection because it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to alter the T-cell epitope peptide to contain no Cys residue in order that no residues be present which could form disulfide bonds.

Applicant's argument in the amendment filed 2/20/03 is moot in light of the new rejection supra. However, with regard to Applicant's comments on page 8 of the said amendment that Rogers et al teaches multiple epitopes isolated from a single allergen and not from two different allergens, the Examiner points to the teaching in Rogers et al supra that the polypeptide can also be constructed using T cell epitopes from unrelated antigens or allergens from diverse sources (especially page 964, lines 60-71 and continuing onto page 965, lines 1-2).

7. Claim 34 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 703-308-0061. The examiner can normally be reached on Monday, Wednesday and Friday afternoon.

If attempts to reach the Examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

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March 16, 2003

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